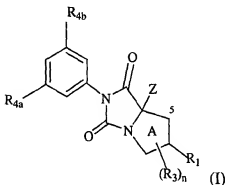


Please add new claims 23 -41 as follows:

23 (New). A compound having the formula (I),



or a pharmaceutically-acceptable salt thereof, in which:

Z is hydrogen, alkyl, or substituted alkyl, except Z is not arylalkyl or heteroarylalkyl;

R<sub>1</sub> is Q-aryl or Q-heteroaryl, wherein Q is -W-(CH<sub>2</sub>)<sub>m</sub>;

W is selected from -O-, -NR<sub>10</sub>-, -S-, -C(=O)-, -CO<sub>2</sub>-, and -CH<sub>2</sub>-;

R<sub>3</sub> is attached to any available carbon atom of ring A and at each occurrence is selected independently of each other R<sub>3</sub> from halogen, alkyl, substituted alkyl, alkenyl, alkynyl, nitro, cyano, OR<sub>8</sub>, NR<sub>8</sub>R<sub>9</sub>, CO<sub>2</sub>R<sub>8</sub>, C(=O)R<sub>8</sub>, C(=O)NR<sub>8</sub>R<sub>9</sub>, NR<sub>8</sub>C(=O)R<sub>9</sub>, NR<sub>8</sub>C(=O)OR<sub>9</sub>, OC(=O)R<sub>8</sub>, OC(=O)NR<sub>8</sub>R<sub>9</sub>, SR<sub>8</sub>, S(O)<sub>q</sub>R<sub>8a</sub>, NR<sub>8</sub>SO<sub>2</sub>R<sub>9</sub>, SO<sub>2</sub>NR<sub>8</sub>R<sub>9</sub>, aryl, heteroaryl, heterocyclo, cycloalkyl, and keto (=O), provided that when R<sub>3</sub> is attached to the atom designated as the C-5 atom of ring A, then R<sub>3</sub> is not aryl or heteroaryl;

R<sub>4a</sub> and R<sub>4b</sub> are selected independently of each other from the group consisting of hydrogen, halogen, alkyl, substituted alkyl, alkenyl, alkynyl, nitro, cyano, hydroxy, alkoxy, substituted alkoxy, phenyloxy, benzyloxy, CO<sub>2</sub>H, C(=O)H, amino, alkylamino, substituted alkylamino, CO<sub>2</sub>alkyl, (C=O)alkyl, and alkylthio;

$R_8$  and  $R_9$  (i) selected independently of each other are hydrogen, alkyl, substituted alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclo; or (ii) taken together form a heterocyclo ring;

$R_{8a}$  is alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclo;

$R_{10}$  is hydrogen, alkyl, or substituted alkyl;

$n$  is 0, 1, or 2;

$q$  is 1, 2, or 3; and

$m$  is 0, 1, 2, 3, or 4.

24 (New). The compound of claim 23, or a pharmaceutically-acceptable salt thereof, wherein:

$Z$  is hydrogen, lower alkyl, or lower alkyl substituted with hydroxy, alkoxy, halogen, cyano, nitro, amino, or alkylamino;

$R_3$  is attached to any available carbon atom of ring A other than T and is selected from halogen, alkyl, substituted alkyl, alkenyl, cyano,  $OR_8$ ,  $NR_8R_9$ ,  $CO_2R_8$ ,  $(C=O)R_8$ ,  $C(=O)NR_8R_9$ ,  $NR_8C(=O)R_9$ ,  $NR_8C(=O)OR_9$ ,  $SR_8$ ,  $S(O)_qR_{8a}$ ,  $NR_8SO_2R_9$ ,  $SO_2NR_8R_9$ , and keto ( $=O$ );

$R_{4a}$  and  $R_{4b}$  are selected independently of each other from the group consisting of hydrogen, halogen, alkyl, alkoxy, cyano, nitro, haloalkyl, and haloalkoxy;

$R_8$  and  $R_9$  selected independently of each other are hydrogen or alkyl, and  $R_{8a}$  is alkyl; and

$m$  is 0, 1, or 2; and

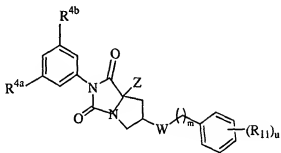
$n$  is 0 or 1.

25 (New). The compound of claim 23, or a pharmaceutically-acceptable salt thereof, wherein:

$W$  is  $-O-$ ,  $-NR_{10}-$ , or  $-S-$ , wherein  $R_{10}$  is hydrogen, lower alkyl, or lower alkyl substituted with  $CO_2H$  or  $CO_2alkyl$ ; and  $m$  is 0, 1, or 2.

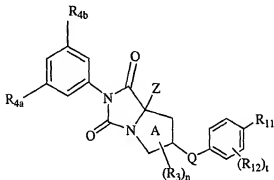
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Cont

26 (New). A compound according to claim 25 having the formula:



or a pharmaceutically-acceptable salt thereof, wherein  $R_{11}$  is selected from halogen,  $C_{1-4}$ alkyl, nitro, cyano, hydroxy,  $C_{1-4}$ alkoxy, haloalkyl, haloalkoxy,  $CO_2H$ ,  $C(=O)H$ , amino,  $C_{1-4}$ alkylamino,  $CO_2C_{1-4}$ alkyl,  $(C=O)C_{1-4}$ alkyl,  $C_{1-4}$ alkylthio, phenyl, phenyloxy, benzyl, and benzyloxy, and  $u$  is 0, 1, or 2.

27 (New). A compound according to claim 23, having the formula,



or a pharmaceutically-acceptable salt thereof, wherein:

$Z$  is hydrogen, alkyl, or alkyl substituted with hydroxy, alkoxy, halogen, cyano, nitro, amino, or alkylamino;

$R_{11}$  is hydrogen, halogen, alkyl, alkoxy, haloalkyl, haloalkoxy, nitro, or cyano;

$R_3$  and  $R_{12}$  are independently selected from alkyl, substituted alkyl, halogen, haloalkyl, haloalkoxy, nitro, cyano, hydroxy, alkoxy, amino, alkylamino, acyl, alkoxycarbonyl, carbamyl, sulfonyl, and sulfonamide;

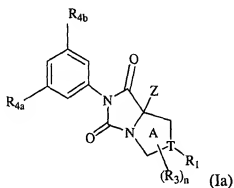
$n$  is 0 or 1; and

$t$  is 0, 1, or 2.

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conf

28 (New). A compound according to claim 27, or a pharmaceutically-acceptable salt thereof, in which  $R_{4a}$  and  $R_{4b}$  are both halogen.

29 (New). A compound having the formula (Ia),



or a pharmaceutically-acceptable salt thereof, in which:

$Z$  is hydrogen, alkyl, alkyl substituted with hydroxy, halogen, cyano, amino, or alkylamino; or when  $R_1$  together with an  $R_3$  group join to form a benzo ring fused to ring A,  $Z$  is arylalkyl or heteroarylalkyl;

$R_1$  is (a)  $-W-(CH_2)_m-Ar$ , or (b) taken together with an  $R_3$  group to form a benzo ring fused to ring A, in which case  $Z$  is arylalkyl or heteroarylalkyl;

$Ar$  is aryl or heteroaryl substituted with zero or one  $R_{11}$  and zero to two  $R_{12}$  groups;

$T$  is  $CR_5$ ;

$W$  is selected from a bond,  $-O-$ ,  $-NR_{10}-$ ,  $-S-$ ,  $-CO_2-$ , and  $-CH(R_{13})-C(=O)-$ ;

$R_3$  is selected independently of each other  $R_3$  from halogen, alkyl, substituted alkyl, alkenyl, nitro, cyano, keto ( $=O$ ),  $OR_8$ ,  $NR_8R_9$ ,  $CO_2R_8$ ,  $(C=O)R_8$ ,  $C(=O)NR_8R_9$ ,  $NR_8C(=O)R_9$ ,  $NR_8C(=O)OR_9$ ,  $OC(=O)R_8$ ,  $OC(=O)NR_8R_9$ ,  $SR_8$ ,  $S(O)_qR_{8a}$ ,  $NR_8SO_2R_9$ ,  $SO_2NR_8R_9$ , aryl, heteroaryl, heterocyclo, and cycloalkyl; and/or one  $R_3$  together with  $R_1$  may join to form a fused benzo ring;

$R_5$  is hydrogen, halogen, alkyl, alkenyl, hydroxy, nitro, cyano, hydroxy, alkoxy, amino, or alkylamino, or  $C_{1-4}$  alkyl optionally substituted with hydroxy, amino, alkylamino, halogen, or cyano;

*B7*  
*cont*  $R_{4a}$  and  $R_{4b}$  are selected independently of each other from the group consisting of hydrogen, halogen, alkyl, nitro, cyano, haloalkyl, and haloalkoxy;

$R_8$  and  $R_9$  (i) selected independently of each other are hydrogen, alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclo; or (ii) taken together form a heterocyclo ring;

$R_{8a}$  is alkyl, substituted alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclo;

$R_{11}$  is hydrogen, halogen, alkyl, hydroxy, alkoxy, amino, alkylamino, haloalkyl, haloalkoxy, nitro, or cyano;

$R_{12}$  is alkyl, substituted alkyl, halogen, haloalkyl, haloalkoxy, nitro, cyano, hydroxy, alkoxy, substituted alkoxy, amino, alkylamino, acyl, alkoxy-carbonyl, carbamyl, sulfonyl, or sulfonamide;

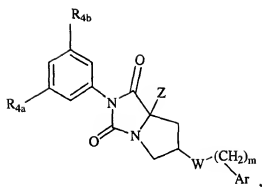
$R_{10}$  and  $R_{13}$  are independently hydrogen, alkyl, or substituted alkyl;

$m$  is 0, 1, 2, 3, or 4;

$n$  is 0, 1 or 2; and

$q$  is 1, 2, or 3.

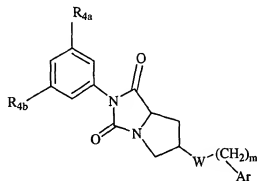
30 (New). A compound according to claim 29, having the formula:



or a pharmaceutically-acceptable salt thereof, wherein Ar is phenyl or isoquinolinyl and Ar is substituted with zero or one  $R_{11}$  and zero to two  $R_{12}$  groups.

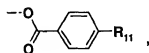
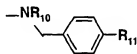
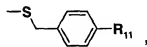
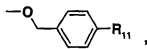
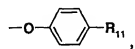
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31 (New). A compound according to claim 30 having the formula,



in which

the groups  $W-(CH_2)_m-Ar$  taken together are selected from:

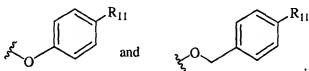


; and

$R_{10}$  is selected from hydrogen, lower alkyl, and lower alkyl substituted with  $\text{CO}_2\text{H}$  or  $\text{CO}_2\text{alkyl}$ , and  $R_{11}$  is selected from hydrogen, bromo, chloro, cyano, and methoxy.

32 (New). A compound according to claim 31, or a pharmaceutically-acceptable salt thereof, in which  $R_{4a}$  and  $R_{4b}$  are both chloro.

33 (New). A compound according to claim 31, in which the groups  $\text{W}-(\text{CH}_2)_m\text{-Ar}$  taken together are selected from:



34 (New). A compound according to claim 33, or a pharmaceutically-acceptable salt thereof, in which  $R_{4a}$  and  $R_{4b}$  are both chloro and  $R_{11}$  is chloro, bromo or cyano.

35 (New). A compound according to claim 23 which is: (I)

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-(4-bromophenoxy)-tetrahydro-pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-(4-bromophenoxy)-tetrahydro-pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-(4-bromobenzyloxy)-tetrahydro-pyrrolo[1,2-c]imidazole-1,3-dione;

(7aR,6R)-2-(3,5-dichloro-phenyl)-6-(4-bromobenzyloxy)-tetrahydro-pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-(4-cyanobenzyloxy)-tetrahydro-pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-benzyloxy-tetrahydro-

pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-(3-bromobenzyloxy)-tetrahydro-

pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-2-(3,5-dichloro-phenyl)-6-(4-[2-cyanophenyl]benzyloxy)-tetrahydro-

pyrrolo[1,2-c]imidazole-1,3-dione;

(7aS,6S)-4-[[2-(3,5-dichloro-phenyl)-1,3-dioxo-hexahydro-pyrrolo[1,2-c]imidazol-6-ylamino]-methyl]-benzonitrile;

(7aS,6S)-N-(4-cyano-benzyl)-N-[2-(3,5-dichloro-phenyl)-1,3-dioxo-hexahydro-pyrrolo[1,2-c]imidazol-6-yl]-acetamide;

(6R,7aS)-[6-(4-bromobenzyloxy)-2-(3,5-dichlorophenyl)-1,3-dioxo-tetrahydro-pyrrolo[1,2-c]imidazol-7a-yl]-acetic acid methyl ester; or

10a-(4-Bromo-benzyl)-2-(3,5-dichloro-phenyl)-10,10a-dihydro-5H-

imidazo[1,5-b]isoquinoline-1,3-dione; or (ii) a pharmaceutically-acceptable salt thereof.

36 (New). A pharmaceutical composition for treating an inflammatory or immune disease comprising (a) at least one compound according to claim 23, or a pharmaceutically acceptable salt thereof, and (b) a pharmaceutically acceptable carrier or diluent.

37 (New). A pharmaceutical composition for treating an inflammatory or immune disease comprising (a) at least one compound according to claim 29, or a pharmaceutically acceptable salt thereof, and (b) a pharmaceutically acceptable carrier or diluent.

38 (New). A pharmaceutical composition comprising (i) at least one compound of claim 23 or a pharmaceutically acceptable salt thereof; (ii) one or more second compositions effective for treating an inflammatory or immune disease; and (iii) a pharmaceutically-acceptable carrier.



39 (New). A method of treating an inflammatory or immune disease comprising administering to a mammal in need of such treatment a therapeutically-effective amount of a composition according to claim 36.

40 (New). The method of claim 39 in which the inflammatory or immune disease is selected from rheumatoid arthritis, chronic obstructive pulmonary disease, psoriasis, and transplant rejection.

41(New). A method of inhibiting a Leukointegrin/ICAM-associated condition which comprises administering to a patient in need thereof an effective amount of a compound of claim 23.

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#### Remarks

Applicant interprets the Office Action as stating that the claims of this application recite separate classes of invention, depending on the selections for r and s (whether five-membered or other-sized rings are recited); for T (whether it is nitrogen or carbon); for Y (whether it is N or CH); for M (whether it is N or CH); L and K (whether they are nitrogen or sulfur); and Q (whether it is O, S, or N, or another linker group such as an alkylene or sulfonyl group.)

The Office Action requests that the applicant elect one of these for prosecution as well as a single species, falling in the elected group. Applicant provisionally elects, with traverse, the species of Example 5, having the formula: